REMARKS

Claims 12-14 have been added. Support for these claims can be found throughout the specification, for example, page 12. No new matter has been added. Applicant respectfully requests entry of the amendments and reconsideration of the application in view of the amendments and the following remarks.

Rejection Under 35 U.S.C. § 103

Claims 1-11 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Naughton et al in view of Vyakarnam et al taken with Hinsch et al and Japanese patent 3-23864. Applicant respectfully traverses the rejection.

The present invention is directed to, for example, a matrix for culturing cardiovascular cells to regenerate cardiovascular tissue comprising a sponge made of a bioabsorbable material and a reinforcement made of a bioabsorbable material, and to a method for regenerating cardiovascular tissue comprising seeding cells on said matrix and culturing the cells.

The present invention achieves in at least an embodiment the remarkable effect of obtaining a matrix which allows cells to sufficiently adhere thereto, provides an optimum scaffold for cell proliferation, maintains satisfactory blood flow resistance in vivo till autogeneous tissue is regenerated, and is ultimately decomposed and absorbed in vivo.

Cited References

Naughton discloses stromal cell-based three-dimensional living stromal tissues that can be used as corrective structures in the body, including tubular structures that can be used to replace or repair blood vessels (column 6, lines 55 to 58). Naughton discloses examples of biodegradable matrices, such as of polyglycolic acid, in column 9, lines 59 to 63 in the specification. A collagen sponge is disclosed in column 9, line 42 in the specification. Naughton discloses that, in addition to fibroblasts and other stromal cells, smooth muscle cells, endothelial cells and the like can also be used (column 4, lines 23 to 30).

Vyakarnam discloses porous bioabsorbable polymer foams that have a gradient in composition and/or microstructure (column 1, lines 8 to 13, and column 4, lines 10 to 25). These foams are useful for regeneration of tissues such as vascular grafts (column 3, lines 13 to 23). Vyakarnam also discloses, in column 9, lines 53 to 56, bioabsorbable polymers such as

copolymers of lactide. In column 4, line 67 to column 5, line 2, Vyakarnam discloses foams with pore size of 30 μm to 50 μm and 100 μm to 200 μm in porous gradient.

Hinsch discloses a porous (average pore size of 10-200 μm) implant suitable for growing blood vessels, the implant being made of a resorbable polymer such as polylactide, in which at least one textile reinforcement made of resorbable plastic is embedded (abstract; page 2, lines 1 to 4 and 43 to 45; and page 3, lines 8 to 13).

JP3-23864 discloses a filler to be transplanted in vivo, the filler comprises a collagen sponge in which a fibrous bioabsorbable polymer (poly-L-lactic acid) is embedded therein (Abstract). This filler accelerates the growth of fibroblasts, maintains its shape and strength for a duration enough long for medical treatment, and is absorbed in vivo after treatment.

No Motivation to Combine Naughton/Vyakarnam with Hinsch/JP3-23864

The Examiner has asserted that it would have been obvious to form the biodegradable polyglycolic acid copolymer tubular structure of Naughton with the biodegradable foam of Vyakarnam, and it would have been further obvious to reinforce the foam with fibers as suggested by Hinsch and JP3-23864. However, the present invention is not obvious from the cited references for the reasons described below.

Naughton teaches a biodegradable matrix having a tubular structure that can be used to replace or repair a blood vessel. However, it does not disclose a reinforcement for reinforcing the biodegradable matrix.

Vyakarnam teaches a porous bioabsorbable polymer foam having a tubular structure used for regenerating blood vessels, etc., and harvesting the cells by seeding them onto the foams (column 18, from line 58). However, it does not disclose a reinforcement made of a biodegradable polymer.

The implant of Hinsch is made of a resorbable polyester such as polylactide or the like, is used for growing blood vessels, is porous having pores of which the average pore diameter is 10-200 μm, and has a textile reinforcement formed of resorbable plastic embedded therein. Hinsch is different from the present invention in that it does not teach that cells are grown by being seeded on the implant.

The filler disclosed in JP3-23864 uses poly-L-lactic acid. However, JP3-23864 is different from the present invention in that this filler is embedded in vivo as is, i.e., without

seeding and growing cells, and that the filler is not used for regenerating blood vessel or the like tissues.

Considering the above, both Naughton and Vyakarnam employ "tissue engineering" in which tissues are regenerated by seeding, culturing, and growing autogenous cells on a matrix, and the regenerated tissues are transplanted in vivo. However, Hinsch and JP3-23864 relate to implants used by simply embedding the implants in. vivo without seeding, culturing, growing the cells onto a matrix. Therefore, they are fundamentally different from Naughton and Vyakarnam.

In other words, Naughton and Vyakarnam, which disclose a method for regenerating tissues by employing tissue engineering, are totally different from Hinsch and JP3-23864, which do not employ tissue engineering, in terms of the techniques used, role and function thereof, etc. Therefore, there is no motivation in Naughton and Vyakarnam to combine the teachings thereof with those of Hinsch and JP3-23864. In other words, it would not have been obvious to arrive at employing "a reinforcement made of a biodegradable material" with "the foam formed of a biodegradable material" of Naughton and Vyakarnam.

None of the References Disclose the Subject Matter of Claims 3-5

The invention claimed in Claims 3-5 is directed to a matrix comprising a sponge and reinforcement suitable for the matrix to regenerate an artery, vein, heart valve, or pericardia (claims 3, 4 and 5). The present invention defines a sponge and reinforcement suitable for the regeneration of specific cardiovascular tissues. None of the cited references include such disclosures or teachings.

Naughton and Vyakarnam disclose a matrix for blood vessels (artery and vein) and like tubular structures. However, they neither teach nor suggest that such a matrix can be used for regeneration of a "heart valve" or "pericardia" as recited in claims 5, 9 and 10 of the present invention. Therefore, these claims are unobvious.

Furthermore, as described in Example 1 in the present specification, artificial blood vessels with and without a reinforcement exhibited significant differences in working-effects when implanted in the inferior vena cava of a young dog. Specifically, the matrix not reinforced with poly-L-lactide fiber ruptured one week after substitution and the dog suddenly died. In contrast, no obliteration by rupture was found in the matrix with a reinforcement of the present invention and revealed regeneration of the autogenous blood vessel in agreement with the

transplantation site. Even a skilled artisan would not have expected such a remarkable effect from the above-mentioned cited references.

For the reasons described above, Applicant respectfully submits that the present invention is not obvious from the cited references, and requests that the pending claims be allowed.

New Claims

Claims 12-14 have been added. These claims recite "seeded with a cell culture and cultured in vitro." As explained above, none of the references teaches or even suggests a reinforce matrix seeded and cultured in vitro. For example, Hinsch et al and JP3-23864 simply teach embedding implants in vivo. Thus, the references could not lead to the invention recited in Claims 12-14. It is respectfully submitted that these claims are allowable.

CONCLUSION

In light of the Applicant's amendments to the claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: Feb. 8, 2005

By: _____

Katsuhiro Arai
Registration No. 43,315
Attorney of Record
Customer No. 20,995
(949) 760-0404

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